PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 13 APR 2004
WIPO PCT

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
021008woMege		

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 02/03992	10.04.2002	18.01.2002

International Patent Classification (IPC) or both national classification and IPC
A01K67/033

Applicant
EVOTEC NEUROSCIENCES GMBH et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.08.2003	08.04.2004

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 02/03992

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-25 as originally filed

Claims, Numbers

1-17 as originally filed

Drawings, Sheets

1-7 as originally filed

Sequence listing part of the description, pages:

1-2, filed with the letter of 11042003,

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority in written form.

   ☒ furnished subsequently to this Authority in computer readable form.

   ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	9-11,15,16
	No:	Claims	1-8,12-14,17
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-17
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations

   see separate sheet

V. **Reasoned statement** (Continuation)

1. CITATIONS

Reference is made to the following documents:

D1: Tschäpe J-A et al (2001) ABSTRACT OF PAPERS PRESENTED AT THE 2001 MEETING ON NEUROBIOLOGY OF DROSOPHILA, Cold Spring Harbor, p.201, "The Drosophila Mutant Löchrig (loe) - Neurodegeneration and Cholesterol Metabolism".

D2: WO0120003

D3: Fortini M et al (2000) Trends in Genetics, vol. 16, pp.161-167, "Modeling human neurodegenerative diseases in Drosophila: On a wing and a prayer".

D4: WO03028446

D5: WO02057455

N.B. D4 and D5 have been cited in the International Search Report as a E documents. Should the present application be entered into regional phase before the EPO, D4 and D5 might be relevant against novelty.

2. NOVELTY (Art. 33(2) PCT)

2.1. The application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-8, 12-14 and 17 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT) for the following reasons: D1 discloses the identification and characterisation of the Drosophila löchrig mutant. It indicates that said mutants show age-dependent neurodegeneration, that is enhanced by mutation of Drosophila APP homolog. The löchrig locus is identified as mutant of the gamma-AMP-activated protein kinase gene. Processing of Appl is described as affected (less secreted form). In conclusion, said löchrig mutant Drosophila strain is proposed as model to study cholesterol and APP metabolic interaction, and understand pathogenesis of AD.

2.2. Similarly, the present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1, 8 and 12 is not new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT) for the following reasons: D2 describes variants and mutants of porcine and human AMPKg, and suggests and claims to make transgenic animals with said variants and mutants.

3. INVENTIVE STEP (Art. 33(3) PCT)

The present application does not satisfy the criterion set forth in Article 33(3) PCT because the subject-matter of claims 9-17 does not involve an inventive step (Art.33(3) PCT and R.65(1)(2) PCT) for the following reasons:

3.1. Document D1 is considered to represent the most relevant state of the art and discloses the identification and characterisation of the Drosophila löchrig mutant. It indicates that said mutants show age-dependent neurodegeneration, that is enhanced by mutation of Drosophila APP homolog. The löchrig locus is identified as

mutant of the gamma-AMP-activated protein kinase gene. Processing of Appl is described to be affected (less secreted form). In conclusion, said löchrig mutant Drosophila strain is proposed as model to study cholesterol and APP metabolic interaction, and understand pathogenesis of AD.

3.2. The technical difference between said closest prior art and the subject-matter of claims 9-11 differs in that said löchrig Drosophila further expresses a gene coding for a modified version of an amyloid precursor protein, or for a modified version of AMPKg.

3.3. The technical effect of said difference is analysis of the interaction of the löchrig locus with a modified version of a gene.

3.4. The objective problem solved by the subject matter of claims 9-11 may therefore be regarded as the provision of a system for analysing the interaction of the löchrig locus with a modified version of a gene.

3.5. The proposed solution is the provision of löchrig Drosophila further expressing a gene coding for a modified version of a gene, e.g. a modified version of an amyloid precursor protein gene, or a modified version of AMPKg gene.

3.6. This solution cannot however be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:
Document D3, a review article, describes Drosophila models of neurodegeneration. It notably mentions reverse genetics as applicable investigation tool for studying interaction of genetic loci (see e.g. p.165 par.3: rescue of Drosophila Appl-homozygous mutants by expression of human beta-APP). It mentions the possibility to test candidate modifier genes, therapeutic compounds, ...

3.7. The present application does therefore not satisfy the criterion set forth in Article 33(3) PCT since the subject-matter of claims 9-11 does not involve an inventive step (Rule 65(1)(2) PCT).

3.8. Furthermore claims 12-17 lack essential technical features. Besides objections under Art. 5 (disclosure) and 6 (clarity and support) PCT, this leads to objections under Art.33(3) PCT (inventive step) since their subject-matter cannot be considered to solve an objective problem.